Drug Utilization Review (DUR) Newsletter

COLORADO
Department of Health Care Policy & Financing

Select HCPF Medication Use Policy Updates

What is DUR and what does it do?

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Click to access the HCPF Pharmacy Resources Page and Colorado Preferred Drug List (PDL)

Is your practice site address out of date? See page 2

Federal requirements

The Omnibus Budget Reconciliation Act of 1990 (OBRA '90) requires each state Medicaid agency to establish a Drug Utilization Review (DUR) Board as a part of its program to evaluate prospective and retrospective medication use for its Medicaid population.

Federal law requires Medicaid DUR Boards and programs to conduct, but not be limited to, the following activities:

- Medication use review and application of medication use standards
- Ongoing interventions for physicians and pharmacists
- Evaluation of previous interventions for quality improvement

HCPF and the Colorado Evidence-based DUR (CO-DUR) Program

The Department of Health Care Policy & Financing (HCPF) contracts with the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences to help carry out many DUR activities for Health First Colorado, Colorado's Medicaid program and meet federal and state requirements for DUR. Some examples of these activities are:

- Facilitating and maintaining a DUR Board that meets publicly to discuss medication use criteria and make policy recommendations to HCPF
- Reviewing and developing medication use criteria and making recommendations based on current evidence
- Recommending guidelines that govern predetermined standards for prospective DUR (ProDUR)
- In collaboration with HCPF, conducting policy-relevant analyses using Medicaid pharmacy claims data and using the findings to make policy recommendations
- Under the direction of the Department, maintaining a provider outreach program in the form of mailed letters for the purpose of educating practitioners about common drug therapy problems
- DUR Team members:
  - Jeff Taylor, PharmD (DUR Pharmacist – HCPF)
  - Julia Rawlings, PharmD, BCPS, CPPS (CO-DUR)
  - Robert Lee Page II, PharmD, MSPH, BCPS, CGP (CO-DUR)
  - Gina Moore, PharmD, MBA (CO-DUR)
  - Heather Anderson, PhD (CO-DUR)
  - Garth Wright, MPH (CO-DUR)

Interested in serving as a member of the Colorado DUR Board?

Click to access the Colorado Drug Utilization Review Board Page

DUR Board members (4 physicians, 4 pharmacists and 1 industry representative) serve in an advisory capacity to the Department and make recommendations regarding drug utilization, educational interventions, and application of standards. The DUR Board also provides recommendations to the Department regarding prior authorization criteria for a wide range of drug classes and medications.

Physicians and pharmacists are being recruited on a continuous basis to fill positions on the Colorado DUR Board. If you are interested in learning more about these professional opportunities, send an inquiry to Jeff Taylor (jeffrey.taylor@state.co.us) or Julia Rawlings (julia.rawlings@state.co.us). If there are no Board openings at the time you apply, the Department will keep your information on file and may contact you in the future regarding your interest in DUR Board openings as they arise.

The next DUR Board meeting will be held virtually on February 9, 2021 from 1:00 to 5:00pm. Details will be posted on the Colorado DUR Board Page *(link in blue box above)* prior to the meeting date.

Take a few minutes to update your practice site information!

Have you changed jobs since you first enrolled with Health First Colorado? Has it been a while since you updated your practice site address? If you suspect that your information is out of date, take a few minutes to submit an online **Provider Maintenance request**.

The DUR team prepares educational letters that are mailed each quarter to individual prescribers. These retrospective DUR letters are *member-specific*. They contain information about potential opportunities to maximize the safety of medication use and help you avoid common problems related to drug therapy. If your mailing address is out of date, you're missing out on these customized communications!

After you submit your address change request you will receive a 6-digit tracking number (ATN). Once approved, the new address will show up in your account. The full process may take up to four weeks.

Type carefully! Change requests cannot be returned for corrections, so if you make an error you will need to start over and submit a new request.

A **quick guide** is available at https://www.colorado.gov/pacific/hcpf/prov-maintenance

And while you're updating address information…

Keep in mind that the information associated with your **National Provider Identifier (NPI)** also needs to stay current. Update your NPI address and profile at https://nppes.cms.hhs.gov/#/

August 2020 DUR Board Meeting PDL Topics

- Erythropoesis Stimulating Agents
- Anticoagulants
- Anticonvulsants
- Bone density agents
- Oral contraceptives
- Colony Stimulating Factor Agents
- Diabetes Agents (non-insulin)
- Insulin
- GI Motility Agents
- Hereditary Angioedema Agents
- Overactive Bladder Agents
- Prenatal Vitamins/Minerals
- Stimulants and Related Agents
- Ophthalmic Immunomodulators

The DUR Telephone Consultation Service

- DUR provides as-needed telephone consults with physicians in two different specialties:
  - **Child and Adolescent Psychiatry**
  - **Pain Management**
- If you are an enrolled provider for Health First Colorado, you are qualified to use this service
- A consult may occur if:
  - A member meets certain criteria established by HCPF and evaluated by Magellan Rx Management, the pharmacy benefits manager (PBM) for Health First Colorado
  - A provider requests a consult when speaking with Magellan Rx Management

November 2020 DUR Board Meeting PDL Topics

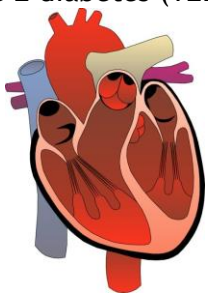
- Hepatitis C Virus Treatments
- Oral fluroquinolones
- Inhaled Antibiotics
- Antidepressants
- NSAIDs
- Pulmonary HTN Agents
- Antipsoriatics
- Pancreatic Enzymes
- Triptans/Migraine Treatments
- Proton Pump Inhibitors
- Antiemetics
- *H. Pylori* Treatments
- Antiplatelet Agents
- Methotrexate Products
- Antihyperuricemics
- Ulcerative Colitis
- Self-administered Epinephrine
- Targeted Immune Modulators

Welcome Julia Rawlings, PharmD

Julia Rawlings joined the DUR team as the DUR Clinical Specialist in July 2020. Julia has experience in community pharmacy practice, primary care clinical pharmacy services, clinical research, and medication safety. She completed her undergraduate degree at CU Boulder and received a Doctor of Pharmacy degree from the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences in 2004. Her most recent position before returning to her alma mater as an employee and member of the faculty was Clinical Pharmacy Specialist in Medication Safety for Kaiser Permanente Colorado. Julia enjoys teaching and mentoring PharmD and pre-pharmacy students, exploring the science of patient safety and quality improvement, and being a part of the Health First Colorado DUR team. She is board certified in pharmacotherapy (BCPS) and a certified professional in patient safety. Outside of work Julia enjoys playing piano, hiking, calligraphy, travel and photography.

Second-Generation Diabetes Medications: More Than Just Glucose Lowering

Despite major therapeutic advances leading to improved outcomes over the past two decades, cardiovascular (CV) disease remains the leading cause of morbidity and mortality in patients with type 2 diabetes (T2D).[1,2]



Many providers are quite familiar with the first-generation diabetes medications in the management of T2D for hyperglycemic control, which consist of metformin, insulin, and sulfonylureas and have been on the market for several decades. Since 2000, four new classes of diabetes drugs or "second-generation" diabetes agents have been approved by the Food and Drug Administration (FDA) for T2D management. In 2005, the FDA approved amylin analogs and glucagon-like peptide-1 (GLP-1) receptor agonists, the dipeptidyl peptidase 4 (DPP-4) inhibitors in 2006, and sodium-glucose co-transporter-2 (SGLT-2) inhibitors in 2013.[3,4]

Since 2007, the CV benefits of certain second-generation diabetes drugs were suspected but not yet proven. Not until 2017 with the publication of the Empagliflozin Reduces Mortality in Patients With Type 2 Diabetes at High Cardiovascular Risk (EMPA-REG OUTCOME) trial did empagliflozin became the first of the second-generation agents to demonstrate significant reductions in CV death in adults with T2D and established CV disease.[5] Since this time, similar benefits have been proven with dapagliflozin and canagliflozin.[6,7] The GLP-1 agonists, dulaglutide, liraglutide, and semaglutide have also been shown to reduce major CV events in adults with T2D and established CV disease.[8-10]

In 2019 and 2020, additional data were published with both dapagliflozin and empagliflozin, respectively, demonstrating significant reductions in morbidity and mortality in patients with HFrEF independent of a T2D diagnosis.[11,12]

Based on these significant positive outcomes, the American Diabetes Association (ADA) updated their 2020 Management Guidelines to specifically recommend the SGLT-2 inhibitors and GLP-1 receptor agonists for those with compelling indications such as heart failure with reduced ejection fraction (HFrEF) and those with atherosclerotic cardiovascular disease (ASCVD).[3]

However, while these newer second-generation agents have been shown to have excellent CV clinical benefits, they do have some safety concerns. For example, the DPP-4 inhibitors specifically saxagliptin and aloglipitin have been shown to significantly increase the risk for heart failure (HF) hospitalization independent of a HF diagnosis, alerting the FDA to add this precaution to their respective package labels. Both saxagliptin and aloglipitin should be avoided in patients with a history of HFrEF.[13]

Both the ADA and the American College of Cardiology recommend the consideration of either an SGLT-2 inhibitor (specifically dapagliflozin, empagliflozin, or canagliflozin) or a GLP-1 agonist (specifically dulaglutide, liraglutide, or semaglutide) for patients with established ASCVD and T2D. In patients with HFrEF and T2D, both organizations give first preference to the SGLT-2 inhibitors (specifically dapagliflozin or empagliflozin), followed by the GLP-1 agonists with ASCVD benefits.[3,14]

The tables on pages 5 and 6 summarize the dosing, indications, side effects, contraindications, and clinical considerations for SGLT-2 inhibitors and GLP-1 agonists with proven CV benefits that are currently on the Colorado Preferred Drug List (PDL).[3,14]

Summary of Second-Generation Diabetes Medications Covered on the PDL with Proven CV Benefits in Patients with T2D

(Modified from references 3,14)

Medication	Dose	FDA Indications	Contraindications	Side Effects to Monitor	Clinical Considerations
GLP-1 Agonists					
Victoza® (liraglutide)	0.6mg SC daily; titrate as tolerated to 1.8 mg or maximally tolerated dose	Improve glycemic control in adults with T2D _____ Reduce risk of MI, CVA, or CV death in adults with T2D and CV disease	Pregnancy or breast feeding Personal or family history of medullary thyroid cancer Personal or family history of MEN2	Nausea, vomiting, diarrhea, headache, weakness, or dizziness Hypoglycemia when given with insulin or sulfonylureas Weight loss Injection site reactions	Hypoglycemia risk increased with insulin or sulfonylureas May delay gastric emptying; not recommended in patients with clinically meaningful gastroparesis. This effect is usually transient with longer-acting GLP-1Ras. Care should be taken in patients with prior gastric surgery, including bariatric surgery Diabetic retinopathy complications were reported with semaglutide (injectable), although it is unclear if this is a direct effect of the drug or due to other factors such as rapid improvement in blood glucose control
SGLT-2 Inhibitors					
Farxiga® (dapagliflozin)	10 mg po daily	Improve glycemic control in adults with T2D as an adjunct to diet and exercise _____ Reduce the risk of hospitalization for HFrEF in adults with T2D and established CV disease or multiple CV risk factors _____ Reduce the risk of CV death and hospitalization for HF in adults with HFrEF	eGFR <45 ml/min/1.73 m^2 - use is not recommended for glycemic control _____ eGFR <30 mL/min/1.73 m^2 - use is contraindicated for HFrEF _____ Dialysis _____ Pregnancy or breast feeding	Genital fungal infections _____ Urinary tract infections _____ Euglycemic diabetic ketoacidosis _____ Lower limb ulcerations and soft tissue infections	Discontinue at least 3 days before a planned surgery to prevent postoperative ketoacidosis If HbA1c well-controlled at baseline, or known history of frequent hypoglycemic events, wean or stop sulfonylurea and consider reducing total daily insulin dose by ~20% when starting therapy May contribute to intravascular volume contraction; consider stopping or reducing diuretic dose if applicable Use with caution in patients with prior amputation, severe peripheral neuropathy, severe peripheral vascular disease, or active diabetic foot ulcers or soft tissue infections Possible increased risk of bone fractures (canagliflozin)

Summary of Second-Generation Diabetes Medications Covered on the PDL with Proven CV Benefits in Patients with T2D *(continued)*

Medication	Dose	FDA Indications	Contraindications	Side Effects to Monitor	Clinical Considerations
Invokana® (canagliflozin)	100 mg po daily	Improve glycemic control in adults with T2D as an adjunct to diet and exercise _____ Reduce risk of MI, stroke, or CV death in adults with T2D and CV disease _____ Reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for HFrEF in patients with T2D and diabetic nephropathy with albuminuria	eGFR <30 mL/min/1.73 m^2 - use is not recommended for glycemic control _____ Dialysis _____ Pregnancy or breast feeding	Genital fungal infections _____ Urinary tract infections _____ Euglycemic diabetic ketoacidosis _____ Lower limb ulcerations and soft tissue infections	Discontinue at least 3 days before a planned surgery to prevent postoperative ketoacidosis If HbA1c well-controlled at baseline, or known history of frequent hypoglycemic events, wean or stop sulfonylurea and consider reducing total daily insulin dose by ~20% when starting therapy May contribute to intravascular volume contraction; consider stopping or reducing diuretic dose if applicable Use with caution in patients with prior amputation, severe peripheral neuropathy, severe peripheral vascular disease, or active diabetic foot ulcers or soft tissue infections Possible increased risk of bone fractures (canagliflozin)
Jardiance® (empagliflozin)	10 mg po daily	Improve glycemic control in adults with T2D as an adjunct to diet and exercise _____ Reduce risk of CV death in adults with T2D and established CV disease	eGFR <45 mL/min/1.73 m^2 - use is not recommended _____ Dialysis _____ Pregnancy or breast feeding		

ASCVD: Atherosclerotic Cardiovascular Disease; **CV**: Cardiovascular; **CVA**: Cerebrovascular Accident; **eGFR**: estimated glomerular filtration rate; **GLP-1**: Glucagon-like Peptide-1; **FDA**: Food and Drug Administration; **HFrEF**: Heart Failure with Reduced Ejection Fraction; **HbA1c**: Hemoglobin A1C; **MEN2**: multiple endocrine neoplasia; **MI**: Myocardial Infarction; **PDL**: Preferred Drug List; **PO**: Oral; **SC**: Subcutaneous; **SGLT-2** Sodium-Glucose Cotransporter inhibitor; **T2D**: Type 2 Diabetes

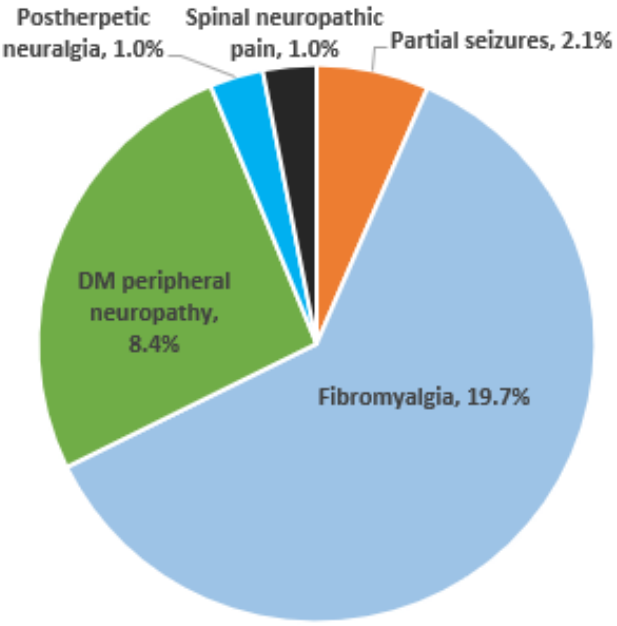
Gabapentin Module Analysis Summary Highlights

The Colorado Evidence-based Drug Utilization Review (CO-DUR) team recently prepared and delivered a clinical module to the Department that characterized use of gabapentinoids (gabapentin and pregabalin) among the Health First Colorado members.

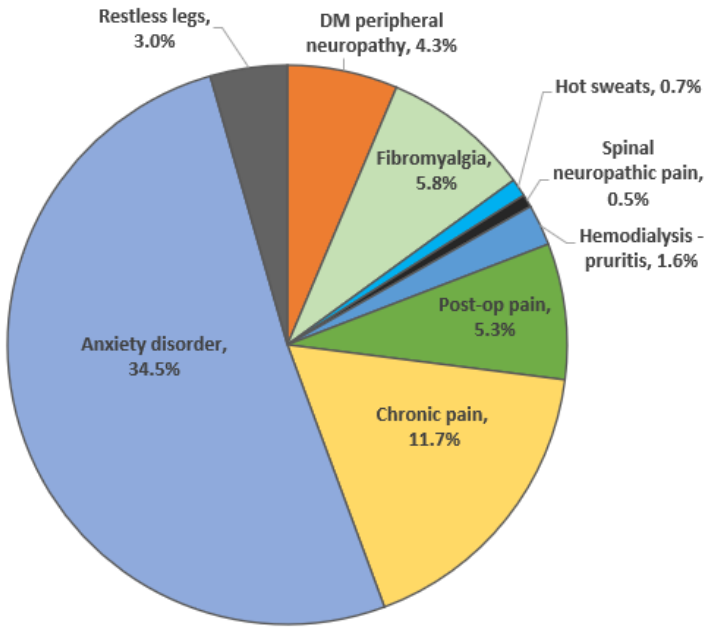
The collective on-label indications for various gabapentinoid preparations (based on labeling for all FDA-approved gabapentin and pregabalin products) include management of postherpetic neuralgia in adults, adjunctive therapy in the treatment of partial onset seizures, diabetic peripheral neuropathy, fibromyalgia, spinal neuropathic pain, and restless leg syndrome.

Diagnoses associated with on-label indications for gabapentin occurred rarely in this analysis.

There are several off-label indications for which gabapentin or pregabalin may be prescribed, many of which are mental health disorders. Mental health disorders were not included in this module due to lacking or controversial evidence without consensus support for use.



ON-label use indications for gabapentin *or* pregabalin
as a percentage of claims
April 1, 2018 – March 31, 2020



OFF-label use indications for gabapentin
as a percentage of claims
April 1, 2018 – March 31, 2020

Of note, certain indications or uses occur both on- and off-label and vary by specific drug formulations. The total percentage of on- and off-label indications is less than 100, reflecting that some potential diagnoses were not included in the analysis.

Also, when evaluating potential diagnoses for the gabapentinoids, members might have more than one diagnosis but may also not have a pre-specified off-label diagnosis, meaning that these agents were being used beyond the documented off-label indications from the literature.

Diagnoses among the population of members receiving gabapentin or pregabalin are varied. The list used by the DUR team comes from clinically known off-label indications, off-label indications described in Micromedex®, and FDA-approved indications with a primary focus on gabapentin.

Using these indications for use, we found that nearly half of individuals receiving either gabapentin or pregabalin had an anxiety disorder. This does not mean these members were being prescribed either medication for an anxiety disorder, but rather that they had the diagnosis in medical claims history and were also receiving either medication. That said, gabapentin is commonly used for anxiety disorders and particularly those that do not respond to traditional therapies.

Chronic pain and other pain disorders (many neuropathic) are also listed as commonly found diagnoses among the population receiving either medication.

- Using the indications included in this module, we found that nearly half of individuals receiving either gabapentin or pregabalin had an anxiety disorder.
- Retrospective (RDUR) letters to providers may be considered to identify members who may be taking higher risk concomitant combinations such as gabapentin, benzodiazepines and skeletal muscle relaxants, for which there is fair evidence of increased risk for CNS and respiratory depression.

References

Second-Generation Diabetes Medications: More Than Just Glucose Lowering

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Characterization of Gabapentinoid Use within Colorado Medicaid Beneficiaries

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